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7	U.S. PATENT DOCUMENTS						
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AMF	AA	4,588,716	DeLuca,, H.F., et al.	05-13-1986			
	AB	4,833,125	Neer, R.M., et al.	05-23-1989			
	AC	5,118,667	Adams, S.W., et al	06-02-1992			
	AD	5,164,368	Recker, R.R., et al	11-17-1992			
	AE	5,510,370	Hock, J.M., et al.	04-23-1996			
	AF	5,565,444	Mizushima, Y., et al.	10-15-1996			
	AG	5,747,456	Chorev, M., et al.	05-05-1998			
	АН	5,821,225	Vickery, B.H., et al.	10-13-1998			
	Al	5,955,425	Morley, P., et al.	09-21-1999			
	AJ	5,977,070	Piazza, C.T., et al.	11-02-1999			
V	AK	6,660,468 B1	Manolagas, et al.	12-09-2003			
AMF	AA2	US 2002/0137209 A1	Kousteni, et al.	09-26-2002			
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	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)				
AMF	AR	Aarden, E.M., et al., "Function of Osteocytes in Bone," J. Cell. Biochem. 55: 287-299 (1994).			
	AS	Amling, M., et al., "Bcl-2 Lies Downstream of Parathyroid Hormone-related Peptide in a Signaling Pathway that Regulates Chondrocyte Maturation During Skeletal Development," Journnal of Cell Biology 136: 205-213 (1997).			
	AT	Bellido, T., et al., "Overexpression of Bcl-2 Renders Osteoblastic Cells Refractory to Glucocortcoid-Induced Apoptosis," Bone 23: S324 (1998).			
	AU	Bursch, W., et al., "Determination of the Length of the Histological Stages of Apoptosis in Normal Liver and in Altered Hepatic Foci of Rats," Carcinogenesis 11: 847-853 (1990).			
	AV	Dempster, D.W., et al., "Anabolic Actions of Parathyroid Hormone on Bone," Endocrine Reviews 14: 690-691 (1993).			
	AW	Dobnig, H., et al., "Evidence that Intermittent Treatment with Parathyroid Hormone Increase Bone Formation in Adult Rats by Activation of Bone Lining Cells," Endocrinology 136: 3632-3638 (1995).			
	AX	Finkelstein, J.S., et al., "Prevention of Estrogen Deficiency-Related Bone Loss With Human Parathyroid Hormone-(1-34)," JAMA 280: 045-1030 (1998).			
	AY	Franceschi, R.T., et al., "Regulation of Type I Collagen Synthesis by 1,25-Dihydroxyvitamin D3 in Human Osteosarcoma Cells," Journal of Biological Chemistry 263: 18938-18945 (1988).			
	AZ	Hsu, S., et al., "Color Modification of Diaminobenzine (DAB) Precipitation by Metallic Ions and its Application for Double Immunohistochemistry," J. of Histochemistry and Cytochemistry 30: 1079-1082 (1982).			
	AR2	Jilka, R.L., "Parathyroid Hormone-Stimulated Development of Osteoclasts in Cultures of Cells from Neonatal Murine Calvaria," <i>Bone 7</i> : 29-40 (1986).			
\bigvee	AS2	Jilka, R.L., et al., "Increased Osteoclast Development After Estrogen Loss: Mediation by Interleukin-6," Science 257: 88-91 (1992).			
AMF	AT2	Jilka, R.L., et al., "Linkage of Decreased Bone Mass with Impaired Osteoblastogenesis in a Murine Model of Accelerated Senescence," The Journal of Clinical Investigation 97: 1732-1740 (1996).			

EXAMINER /Anne Marie Falk/	DATE CONSIDERED 09/25/2006

PTO-1449 REPRODUCED	OUR DOCKET NO. 3650.1004-008 FIRST NAMED INVENTOR Stavros C. Manolagas APPLICATION NO. 10/743,360 FILING DATE December 22, 2		
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	EXAMINER Not Assigned	CONFIRMATION NO.	GROUP 1614

_	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)				
AMF AU2		Jilka, R.L., et al., "Loss of Estrogen Upregulates Osteoblastogenesis in the Murine Bone Marrow, Evidence of Autonomy from Factors Released During Bone Resorption," The American Society for Clinical Investigation, Inc. 101: 1942-1950 (1998).			
	AV2	Jilka, R.L., et al., "PTH Increases Bone Formation by Postponing Osteoblast Apoptosis, Not By Increasing Precursor Proliferation," Bone 23: S519 (1998).			
	AW2	Jilka, R.L., et al., "Osteoblast Programmed Cell Death (Apoptosis): Modulation by Growth fctors and Cytokines," Journal of Bone and Mineral Research 13(5): 793-802 (1998).			
	AX2	Kato, Y., et al., "Establishment of an Osteocyte-Like Cell Line, MLO-Y4," Journal of Bone and Mineral Research 12: 2014-2023 (1997).			
	AY2	Lane, N.E., et al., "Parathyroid Hormone Treatment Can Reverse Corticosteroid-induced Osteoporosis," Journal of Clinical Investigation 102: 1627-1633 (1998).			
	AZ2	Leaffer, D., et al., "Modulation of Osteogenic Cell Ultrastructure by RS-23581, an Analog of Human Parathyroid (PTH)-Related Peptide-(1-34), and Bovine PTH-(1-34), Endocrinology 136(8): 3624-3631 (1995).			
	AR3	Lee, K., et al., "Parathyroid Hormone-Related Peptide Delays Terminal Differentiation of Chondrocytes During Endochondral Bone Development," Endocrinology 137: 5109-5118 (1996).			
	AS3	Manolagas, S.C., et al., "Bone Marrow, Cytokines, and Bone Remodeling: Emerging Insights into the Pathophysiology of Osteoporosis," New England Journal of Medicine 332: 305-311 (1995).			
	AT3	Parfitt, A.M., et al., "Bone Histomorphometry: Standardization of Nomenclature, Symbols, and Units," Journal of Bone and Mineral Research 2: 595-610 (1987).			
	AU3	Reeve, J., et al., "Anabolic Effect of Human Parathyroid Hormone fragment on Trabecular Bone in Involutional osteoporosis: a Multicentre Trial," British Medical Journal 280: 1333-1390 (1980).			
lacksquare	AV3	Reeve, J., et al., "Anabolic Effect of Low Doses of a Fragment of Human Parathyroid Hormone on the Skeleton in Postmenopausal Osteoporosis," Lancet 1:1035-1038 (1976).			
MF	AW3	Stewart, A.F., "PTHrP(1-36) as a Skeletal Anabolic Agent for the treatment of Osteoporosis," Bone 19: 303-306 (1996).			

EXAMINER	/Anne Marie Falk/	DATE CONSIDERED	09/25/2006
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PTO-1449 REPRODUCED INFORMATION DISCLOSURE CITATION IN AN APPLICATION July 7, 2004 (Use several sheets if necessary)	OUR DOCKET NO. APPLICATION NO. 10/743,360				
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	EXAMINER Not Assigned	CONFI 9347	RMATION NO.	GROUP 1614	

		OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)				
AMF	AX3	Sudo, H., et al., "In Vitro Differentiation and Calcification in a New Clonal Osteogenic Cell Line D from Newborn Mouse Calvaria," Journal of Cell Biology 96: 191-198 (1983).				
	AY3	Tam, C.S., et al., "Parathyroid Hormone Stimulates the Bone Apposition rate Independently of Its Resorptive Action: Differential Effects of Intermittent and Continuous Administration," Endocrinology 110: 506-512 (1982).				
	AZ3	Thornberry, N.A., et al., "Caspases: Enemies Within," Science 281: 1312-1316 (1998).				
	AR4	Vickery B.H., et al., "RS-66271, a C-Terminally Substituted analog of Human Parathyroid Hormone-Related Protein (1-34), Increases Trabecular and Cortical Bone in Ovariectomized, Osteopenic Rats," Journal of Bone and Mineral Research 11: 1943-1951 (1996).				
	AS4	Weinstein, R.S., et al., "Inhibition of Osteoblastogenesis and Promotion of Apoptosis of Osteoblasts and Osteocytes by Glucocorticoids," The Journal of Clinical Investigation 102: 274-282 (1998).				
	AT4	Wright, S.C., et al., "Activation of CPP32-like Proteases Is Not Sufficient to Trigger Apoptosis: Inhibition of Apoptosis by Agents that Suppress Activation of AP24, but Not CPP32-like Activity," Journal of Experimental Medicine 186: 1107-1117 (1997).				
	AU4	Bellido, et al., "PTH Prevents Glucocorticoid Apoptosis of Osteoblasts and Osteocytes In Vitro: Direct Interference with a Private Death Pathway Upstream of Caspase-3," Abstract. Bone 5: S518: F458 (1998).				
	AV4	Dempster, D.W., "Exploiting and Bypassing the Bone Remodeling Cycle to Optimize the Treatment of Osteoporosis," <i>Journal of Bone and Mineral Research</i> 12(8): 1152-1154 (1997).				
	AW4	Ferretti, J.L., et al., "Perspectives on Osteoporosis Research: Its Focus and Some Insights from a New Paradigm," Calcif. Tissue Int. 57: 399 (1995).				
	AX4	Forrest, S.M., et al., "Characterization of an Osteoblast-like Clonal Cell Line Which Responds to both Parathyroid Hormone and Calcitonin," Calcif. Tissue Int. 37: 51-56 (1985).				
\bigvee	AY4	Gohel, A., et al., "Glucocorticoids Induce Apoptosis in Osteoblasts by the Regulation of Bcl-2, BAX and Other Cell Cycle Factor," Journal of Bone and Mineral Research. Abstract F234: S284 (1997).				
AMF	AZ4	Hughes, D.E., et al., "Apoptosis in Bone Physiology and Disease," MP. Molecular Pathology, BMJ Publishing Group, Vol. 50: 132-137 (1997) London, GB.				

EXAMINER /Anne Marie Falk/	DATE CONSIDERED 09/25/2006

PTO-1449 REPRODUCED	OUR DOCKET NO. 3650.1004-008		PLICATION NO. 743,360	
INFORMATION DISCLOSURE CITATION IN AN APPLICATION	FIRST NAMED INVENTOR Stavros C. Manolagas		FILING DATE December 22, 2003	
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	r	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
AMF	AR5	Hughes, D.E., et al., "Bisphosphonates Promote Apoptosis in Murine Osteoclasts In Vitro and In Vivo," Journal of Bone and Mineral Research 10 (10): 1478-1487 (1995).
	AS5	Iida-Klein, A., et al., "Effects of Calcitonin on 3', 5'-Cyclic Adenosine Monophosphate and Calcium Second Messenger Generation and Osteoblast Function in UMR 106-06 Osteoblast-Like Cells," Endocrinology 130(1): 381-388 (1992).
	AT5	Jilka, R.L., et al., "Dexamethasone Promotes Apoptosis of Osteoblast Progenitors in Murine Bone Marrow Cultures: Antagonism by IL-6 Type Cytokines," Journal of Bone and Mineral Research 12(Supp): S455, Abstract No. S411 (1997).
	AU5	Jilka, R.L., et al., "Increased Bone Formation by Prevention of Osteoblast Apoptosis with Parathyroid Hormone," Journal of Clinical Investigation 104(4): 439-466 (1999).
	AV5	Kameda, T., et al., "Estrogen Inhibits Bone Resorption by Directly Inducing Apoptosis of the Bone-Resorbing Osteoclasts," The Journal of Experimental Medicine 186(3): 489-495 (1997).
	AW5	Lian, J.B., et al., "Species-Specific Glucocorticoid and 1,25 Dihydroxyvitamin D Responsivness in Mouse MC3T3-E1 Osteoblasts: Dexamethadone Inhibits Osteoblast Differentiation and Vitamin D Downregulates Osteocalcin Gene Expression," Endocrinology 138(5): 2117-2127 (1997).
	AX5	Manolagas, S.C., et al., "New Developments in the Pathogenesis and Treatment of Steroid-induced Osteoporosis," Journal of Bone and Mineral Research 14(7): 1061-1066 (1999).
	AY5	Manolagas, S.c., et al., "Opposite Effects of Estrogen on the Life Span of Osteoblasts/Osteocytes Versus Osteoclasts In Vivo and In Vitro: An Explanation of the Imbalance Between Formulation and Resorption in Estrogen Deficiency," Journal of Bone and Mineral Research 14: Abstract No. S169 (1999).
	AZ5	Marotti, G., et al., "Structure-function Relationships in the Osteocyte," Italian Journal of Mineral & Electrolyte Metabolism 4(2): 93-106 (1990).
	AR6	Nishikawa, M., et al., "Bisphosphonates Act on Osteoblastic Cells and Inhibit Osteoclast Formation in Mouse Marrow Cultures," Bone 18(1): 9-14 (1996).
	AS6	Parfitt, A.M., "Bone Forming Cells in Clinical Conditions," Bone, Vol. 1, 351-429, CRC Press, Boca Raton (1996).
AMF	АТ6	Plotkin, L.I., et al., "Bisphosphonates Prevent Glucocorticoid-Induced Apoptosis of Osteocytes in Vitro: a Putative Mechanism Influencing Mechanosensing," Bone 23: S157 (1998).

EXAMINER /Anne Marie Falk/	DATE CONSIDERED 09/25/2006

PTO-1449 REPRODUCED INFORMATION DISCLOSURE CITATION IN AN APPLICATION July 7, 2004 (Use several sheets if necessary)			PLICATION NO. 0/743,360		
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-		OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
AMF	AU6	Plotkin, L.I., et al., "Prevention of Osteocyte and Osteoblast Apoptosis by Bisphosphonates and Calcitonin," Journal of Clinical Investigation 104(10): 1363-1374 (1999).
	AV6	Pompeiano, M., et al., "Onset of Apoptotic DNA Fragmentation Can Precede Cell Elimination by Days in the Small Intestine Villus," Cell Death and Differentiation 5: 702-709 (1998).
	AW6	Sahni, M., et al., "Bisphosphonates Act on Rat Bone Resorption Through the Mediation of Osteoblasts," Journal of Clinical Investigation 91: 2004-2011 (1993).
	AX6	Short, B.G., et al., "Automated Double Labeling of Proliferation and Apoptosis in Glutathione S-Transferase-Positive Hepatocytes in Rats," Journal of Histochemistry & Cytochemistry 45(9): 1299-1305 (1997).
	AY6	Verbeijen, M.H., et al., "Parathyroid Hormone Activates Mitogen-activated Protein Kinase via cAmP-mediated Pathway Independent of Ras," Journal of Biological Chemistry 272(6): 3423-3429 (1997).
	AZ6	Weinstein, R.S., et al., "The Effects of Androgen Deficiency on Murine Bone Remodeling and Bone Mineral Density are Mediated via Cells of the Osteoblastic Lineage," Endocrinology 138(9): 4013-4021 (1997).
	AR7	Schwartz, Z., et al., "Differential Regulation of Prostaglandin E2 Synthesis and Phospholipase Activity by 1,25-(OH)2D3 in Three Osteoblast-like Cell Lines (MC-3T3-E1, ROS 17/2.8, and MG-63)," Bone 13(1): 51-8 (1992).
	AS7	Lane, J.M., et al., "Intermittent Treatment with Human Parathyroid Hormone (hPTH[1-34]) Increased Trabecular Bone Volume but Not Connectivity in Osteopenic Rats," Journal of Bone and Mineral Research 10(10): 1470-1477 (1995)
	AT7	Gunness, M., et al., "Anabolic Effect of Parathyroid Hormone on Cancellous and Cortical Bone Histology," Bone: 14, 277-281 (1993).
	AU7	Hill, P.A., et al., "Multiple Extracellular Signals Promote Osteoblast Survival and Apoptosis," Endocrinology: 138(9), 3849-3858 (1997).
	AV7	Lecka-Czernik, B., et al., "Cellular and Molecular Biomarkers Indicate Precocious In Vitro Senescence in Fibroblasts from SAMP6 Mice," Journal of Gerontology: 52A(6), B331-B336 (1997).
AMF	AW7	Meng, X.W., et al., "Termporal Expression of the Anabolic Action of PTH in Cancellous Bone of Ovariectomized Rats," Journal of Bone and Mineral Research: 11(4), 421-429 (1996).

EXAMINER /Anne Marie Falk/	DATE CONSIDERED 09/25/2006

INFORMATION DISCLOSURE CITATION IN AN APPLICATION July 7, 2004			PPLICATION NO. 0/743,360		
IN AN APPLICATION	FIRST NAMED INVENTOR Stavtos C. Manolagas		FILING DATE December 22, 2003		
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	T	OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
AMF	AX7	Okamoto, Y., "Femoral Peak Bone Mass and Osteoclast Number in an Animal Model of Age-Related Spontaneous Osteopenia," <i>The Anatomical Record</i> : 242, 21-28 (1995).
	AY7	Cornish, J., "An In Vivo Model for the Rapid Assessment of the Local Effects of Parathyroid Hormone on Bone Histomorphometry," <i>Bone: 17(4)</i> Supp., 249S-254S (1995).
	AZ7	Fujibayashi, et al., "Differential Aging Pattern of Cerebral Accumulation of Radiolabeled Glucose and Amino Acid in the Senescence Accelerated Mouse (SAM), a New Model for the Study of Memory Impairment., Biological and Pharmaceutical Bulletin, 17(1):102-105 (1994).
	AR8	Lane, N.E., et al., "Prevention and Management of Glucocorticoid-Induced Osteoporasis", Bulletin on the Rheomatic Diseases, 44(5):1-4 (1995).
AMF	AS8	Lane, N.E., et al., "The Science and Therapy of Glucocorticoid-Induced Bone Loss", Endocrinology and Metabolism Clinics of North American, 27(2):465-483. (1998).
	A18	Lane, N.E., et al., Abstract No. 1757, page \$324 (1997).

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	INFORMATION DISCLOSURE CITATION OF AUGUST 13, 200
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OUR DOCKET NO.
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FIRST NAMED INVENTOR
Stavros C. Manolagas

APPLICATION NO.
10/743,360

FILING DATE
December 22, 2003

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	FOREIGN PATENT DOCUMENTS							
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